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Dopaminergic dysfunction is associated with IL-1 $\beta$ -dependent mood alterations in experimental autoimmune encephalomyelitis

Antonietta Gentile <sup>a, b, 1</sup> ... Diego Centonze <sup>a, b</sup>

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### Highlights

- IL-1 $\beta$  is up-regulated in EAE striatum even in mice with mild-EAE phenotype.
- Mild-EAE mice display depressive-like behavior.
- Reduced release of dopamine in acute phase EAE striatum
- Unbalanced dopaminergic signaling through D1 and D2 receptors
- IL1-ra reverses both mood and striatal neurotransmission alterations.

## Abstract

Mood disturbances are frequent in patients with multiple sclerosis (MS), even in non-disabled patients and in the remitting stages of the disease. It is still largely unknown how the pathophysiological process on MS causes anxiety and depression, but the dopaminergic system is likely involved.

Aim of the present study was to investigate depressive-like behavior in mice with experimental autoimmune encephalomyelitis (EAE), a model of MS, and its possible link to dopaminergic neurotransmission. Behavioral, amperometric and biochemical experiments were performed to determine the role of inflammation in mood control in EAE. First, we assessed the independence of mood alterations from motor disability during the acute phase of the disease, by showing a depressive-like behavior in EAE mice with mild clinical score and preserved motor skills (mild-EAE). Second, we linked such behavioral changes to the selective increased striatal expression of interleukin-1beta (IL-1 $\beta$ ) in a context of mild inflammation and to dopaminergic system alterations. Indeed, in the striatum of EAE mice, we observed an impairment of dopamine (DA) neurotransmission, since DA release was reduced and signaling through DA D1- and D2-like receptors was unbalanced.

In conclusion, the present study provides first evidence of the link between the depressive-like behavior and the alteration of dopaminergic system in EAE mice, raising the possibility that IL-1 $\beta$  driven dysfunction of dopaminergic signaling might play a role in mood disturbances also in MS patients.



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## Keywords

EAE; IL-1 $\beta$ ; Striatum; Dopamine; Depression

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<sup>1</sup> AG and DF are equally contributing first authors.

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